Islet specific Wnt activation in human type II diabetes.

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Public Summary:

Scientific Abstract:
The Wnt pathway effector gene TCF7L2 has been linked to type II diabetes, making it important to study the role of Wnt signaling in diabetes pathogenesis. We examined the expression of multiple Wnt pathway components in pancreases from normal individuals and type II diabetic individuals. Multiple members of the Wnt signaling pathway, including TCF7L2, Wnt2b, beta-catenin, pGSK3beta, TCF3, cyclinD1, and c-myc, were undetectable or expressed at low levels in islets from nondiabetic individuals, but were also upregulated specifically in islets of type II diabetic patients. Culture of pancreatic tissue and islet isolation led to Wnt activation that was reversed by the Wnt antagonist sFRP, demonstrating that Wnt activation in that setting was due to soluble Wnt factors. These data support a model in which the Wnt pathway plays a dynamic role in the pathogenesis of type II diabetes and suggest manipulation of Wnt signaling as a new approach to beta-cell-directed diabetes therapy.